



# **Celulare: transforming healthcare**

**Future Lanthan Hospital Model**

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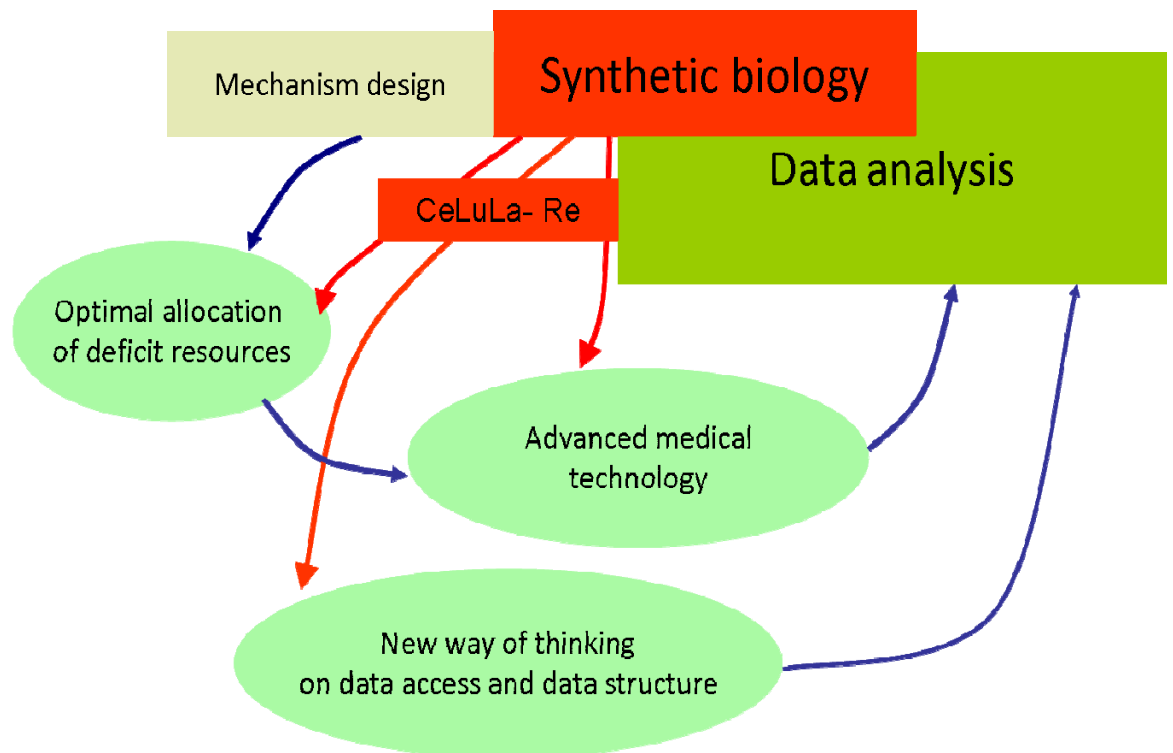
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# Table of contents



## Summary

1. Background – from systems biology through synthetic biology to big data in medicine
2. New application of synthetic biology: transforming healthcare
3. New application of iGEM registry: challenging healthcare for data analysis
4. Solving optimal resource allocation problem with support of synthetic biology, economy and medicine. Step forward to open health
5. Celulare: transforming healthcare for optimal allocation of deficit resources
6. Future Lanthan Hospital - implementation strategy through 'Celulare'
7. Celulare Recommendations
8. Nobel Lanthan Economics with Nobel Human Practice
9. Stable matching and mechanism design through Celulare to Polish healthcare market
10. Closing remarks

Annex 1. Anti selfie mechanism design for smartphone MDs through Celulare

Annex 2. KPD - optimal allocation of deficit resources need access to databases

Annex 3. Celulare – future leaders start here

Annex 4. Creative education - workshops.

## Summary

Nowadays, in the big data era, medicine will be inevitably transformed by systems biology. Rapid developments in deep sequencing, metabolomics and so called "personal medicine" have already changed medical sciences. Hence, we would like to add a valuable contribution to that healthcare transition by proposing a more synthetic biology-oriented approach for medicine. Our project 'Celulare' touches both healthcare transformation for data analysis and optimal allocation of deficit resources. Our question is how to design a hospital only having access to limited resources, equip it in modern technologies (biomedical and IT), and finally how to combine modern technology and pro-ecological design in order to improve the work of healthcare. To address this difficult issue, we developed Future Lanthan Hospital Model, which is aimed to show that recovery of lanthanides (rare earth elements) from electronic waste (smartphones, tablets etc.) by synthetic biology methods, could be a beneficial supporting strategy for a modern hospital. We have proposed integration of a hospital with a supplementary synthetic biology lab, in which lanthanide remediation project could take place. First, such a solution would contribute to the public image of the hospital as a rationally functioning institution with eco-friendly profile. Secondly, it could allow to equip the hospital in modern technologies based on rare-earth metals. Simultaneously, we suggest mechanism design (engineering part of the economy) and the stable matching algorithm allowing better resource-management that would address the needs of the patients. By Future Lanthan Hospital Model we would like to show beneficial changes for society resulted from implementation of modern technologies in medicine and educate people about applications, safety and some security problems related to cutting-edge technologies. In the end we also aim to provide a contribution to the processing of medical data and open source science, since in the era of big data in medicine such measures seems to be necessary for the rapid transformation of the healthcare.

## **Background – from systems biology through synthetic biology to big data in medicine**

A fast and efficient data analysis is expected to transform healthcare globally. Appropriate use of medical data allow us to understand medical history records: signs and symptoms, results of diagnostic and therapeutic procedures as well as digital data from diagnostic devices. However, those are traditional medical data and in the genomic era, access to data from high throughput experiments became something common. As medicine has been transformed by science and technology, we generate much more data than ever before. Furthermore, rapid progress in new technologies enable lowering the costs of healthcare by invention of telemedicine and other branches of medicine based on mobile devices.

The most current challenge in medicine is to process efficiently large amount of data and use them to make rational decisions. It is believed that data analysis is able to provide valuable information and simpler, more direct solutions to medicine-related problems. Unfortunately, there is a surplus of medical data but little knowledge how to use them in an effective way. If we want to advance healthcare with both biomedical technology and engineering itself, generated data need to be analyzed more efficiently. Efficient management of information in the healthcare and optimal allocation of deficit resources also needs data analysis.

As it was mentioned before, due to big data, medicine has started transition to be more system biology and IT-oriented. By convergence of systems biology, the digital revolution and consumer-driven healthcare vision of P4 (predictive, preventive, personalized and participatory), a new "system medicine" emerged. Thus, we are striving to add a next dimension to P4 medicine by proposing a P5 medicine (P4 + programming), which would stipulate synthetic biology approach to medicine.

Although systems biology is about understanding the complex systems, synthetic biology is about applying that knowledge to design and create artificial biological systems. We would

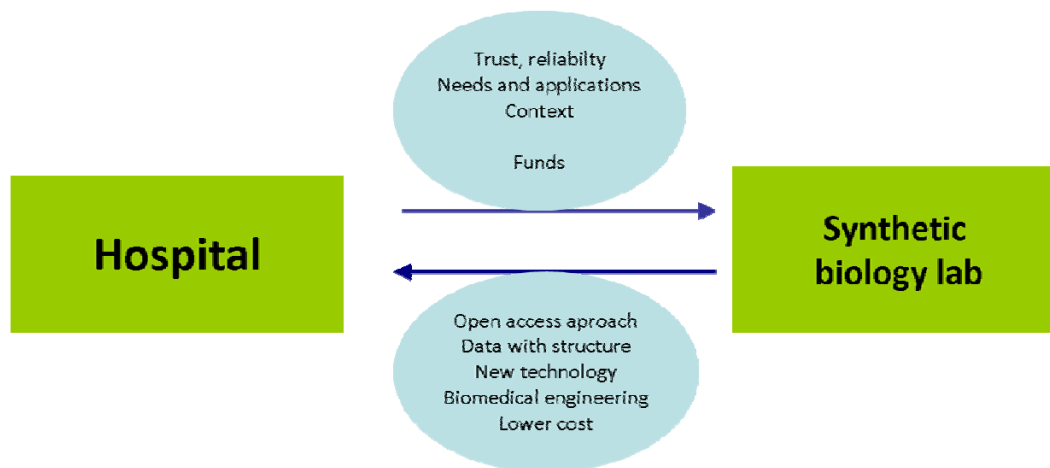
like to change healthcare transformation not only by application of mobile devices, but also invention of programmed biological devices. What is more we have noticed that iGEM data base is a great example of how data are properly structured and used to achieve the important scientific goal – providing the easy-to-use platform to design bigger optimized systems from standardized parts. We would like to recommend this approach as a viable solution for healthcare, making big data more useful for functional analysis and solving complicated problems in medicine.

## **New application of synthetic biology: transforming healthcare**

### *P5 medicine (programming medicine)*

The basic idea behind healthcare transformation to P5 medicine is to integrate synthetic biology lab with hospital (Figure 1). This is sort of start-up strategy with systems impact, which will be presented in the context of a broader healthcare transformation. The cooperation of medical professionals with synthetic biology scientists should provide an opportunity to change mental attitude to open source science and data standards in the medical community. Noteworthy, synthetic biology lab could be less expensive and may allow to rapid implementation of advancements to medical sciences. Potential assets for hospital stemmed from integration of synthetic biology laboratory performing ecological project will be discussed in the next paragraphs. Here we present only a general overview of Future Lanthan Hospital Model with 3 stages to transform healthcare by direct application of synthetic biology approach derived from iGEM competition.

## Hospital with integrated synthetic biology lab



### Start-up approach with Systems Impact

**Figure 1.** Transformation of the healthcare by application of synthetic biology in Future Lanthan Hospital Model – basic idea.

#### Transformation of healthcare:

**First Stage:** iGEM-based data registry and management for medical professionals

**Second Stage:** Lanthan Recycling System For Hospitals (implementation of iGEM Warsaw Team project)

**Third stage:** Future Lanthan Hospital Model in practice (strategy and recommendations for juridical and economical analysis as well as business model).



## **New application of iGEM registry: transformation of healthcare for data analysis**

*Medicine based on standards and sharing - iGEM for MDs (IEDM \_ Internationally Engineered Data Medicine)*

We would like to recommend iGEM registry as a great example of data management for medicine. The fundamental idea of medicine is to help, and philosophy of iGEM registry is to share. As help is connected with openness and sharing, both philosophies are in line. However, medicine for the sake of dealing with sensitive personal data is inherently more distant to the idea of openness. It is crucial to secure private medical records, but this fundamental requirement slows down development in medical data processing. More worryingly, there is no sufficient incentives for the strict data standardization, which is necessary to analyze them in an efficient way. Private information may be shared in only strictly regulated manner, so full openness in medicine is not possible. Nevertheless, medical data should be carefully organized to facilitate development. We believe that carefully done data analysis may allow to share only functional knowledge without compromising personal data. Nowadays, medicine becomes an information science, thus it needs to be 'programmed'. It means that a format similar to programming language is necessary to make data useful for further analysis. This is the reason why we would like to challenge medical community, showing iGEM registry as an example, and in turn initiate cooperation between synthetic biology scientists and medical professionals.

Therefore, to support open health we would like to propose a sort of iGEM competition *for MDs - IEDM \_ Internationally Engineered Data Medicine* to award outstanding MDs for their endeavors to use open science approach and keeping educational open registry (Table 1). For instance, they could be given some grading points in their specialization course or PhD studies for attending IEDM. This could be a new way to show MD professionals the importance of keeping records in a concise and well-described format as well as facilitate their cooperation with science and IT. In case of having not enough time for patients in MDs daily routine, they need additional incentives to keep medical records structured and clear.

We suggest also, that in the next stage of this science competition, MDs should strive to develop procedures simplifying having feedback from patients. Such a strategy will lead to constant evaluation of procedures and ensuring their high quality. It needs to be emphasized that the major goal of that competition is only to improve medical sciences (especially the medical education), excluding any type of interference in treatment protocols. Such security measures should convince both medical professionals and society that openness and collaboration are not in a collision course with protection of personal data. To conclude, we can say that in our view, that open ‘synthetic’ approach is the best way to enrich in future medicine with new exciting ideas.

**Table 1. Comparison between** iGEM registry vs. IEDMs Registry (iGEM Competition for M.Ds). IEDMs main goal is to promote creative medical education and open heath.

iGEM Registry	Educational Open Registry for MDs
<b>Documentation &amp; Characterization:</b> ‘parts and devices are user-tested and characterized.	<b>New way for documentation and characterization of medical procedures:</b> Algorithms of treatment are described in standard format resembling programming language.  Diagnostic and therapeutic procedure not strictly defined by recommendation, but based on individual MD ‘s experience are characterized and described in standard format.
<b>BioBrick standard:</b> usage of standard format. ‘Assembling two or more basic parts results in a new, composite part.’	<b>MedicBrick format</b> usage of standard format based on algorithmical principles inspired by programming languages and BioBrick standards.

<p><b>The Catalog of Parts and Devices:</b> ‘many ways to find parts: the catalog has been improved to allow to browse collection by part type, chassis, function or by several other ways.’</p> <p>We made categories much more important in terms of classifying parts to form the basis of the catalog system</p>	<p><b>Functional catalog:</b> many ways to find diagnostic and therapeutic procedures by functional linkage.</p> <p>Classification focused on health not on arbitrary defined disease.</p>
<p><b>Open Medical Community:</b> ‘Wiki tools allow user to edit entries, see recent changes, etc. Part tools can be used to edit the database information about a given part’.</p> <p>‘As part of the synthetic biology community's effort to make biology easier to engineer.’</p>	<p><b>Open Medical Community:</b> Wiki based tools with access only for MDs. Open source editing in medical professionals’ communities.</p> <p>The goal is to make medicine information science more accessible to program procedures.</p>

## Solving optimal resource allocation problem with engineering part of biology, economics and medicine. Step forward to open health.

In previous section we presented the bottom-up strategy to make medical community and society more open for data analysis and open source movement. In the next stage of healthcare transformation, it is crucial to set perspective for rational design of healthcare institutions. We would like to suggests some concepts for integration of novel tools allowing to solve optimal allocation problems in healthcare market and to equip institution with modern devices. Proposed tools are derived from engineering part o biology, medicine and economy.

### **Tools:**

**Synthetic biology** is the basic tool in our comprehensive strategy. The ultimate goal of this discipline is to design new organisms with more optimized genome. The aim is to provide efficient tools to engineer into biological devices which may find direct and indirect applications in medicine, allowing to lower the costs of medical procedures and technologies. Cooperation between synthetic laboratory and hospital may facilitate the implementation of these changes. In our strategy we consider synthetic biology also in the categories of tools aimed at supporting open source science movement in medicine.

### **Medical technology (medicine)**

Medical technology provides versatile tools which may be used to lower the cost of healthcare management and provide more accessible care for everyone. Telemedicine allows MDs to focus on most urgent cases on site, remaining education of patients, extended rehabilitation and some simple diagnostic for teleservices. Some typical medical devices (robots, lasers) are expected to work in more efficient way. Importantly, some smartphone-based medical technologies may lower overall costs and ensure easier access to diagnostics. Effective electronic managing system will be ensured only if devices are well integrated in the hospital.

### **Mechanism design (economics)**

The aim is to show comprehensive strategy for making modern healthcare more accessible. We would like to imply that mechanism design is the optimal way to achieve our goal – to provide a comprehensive strategy to create more accessible healthcare. To give general insight what mechanism design really is, one can cite Eric Maskin who has laid foundations for mechanism design theory:

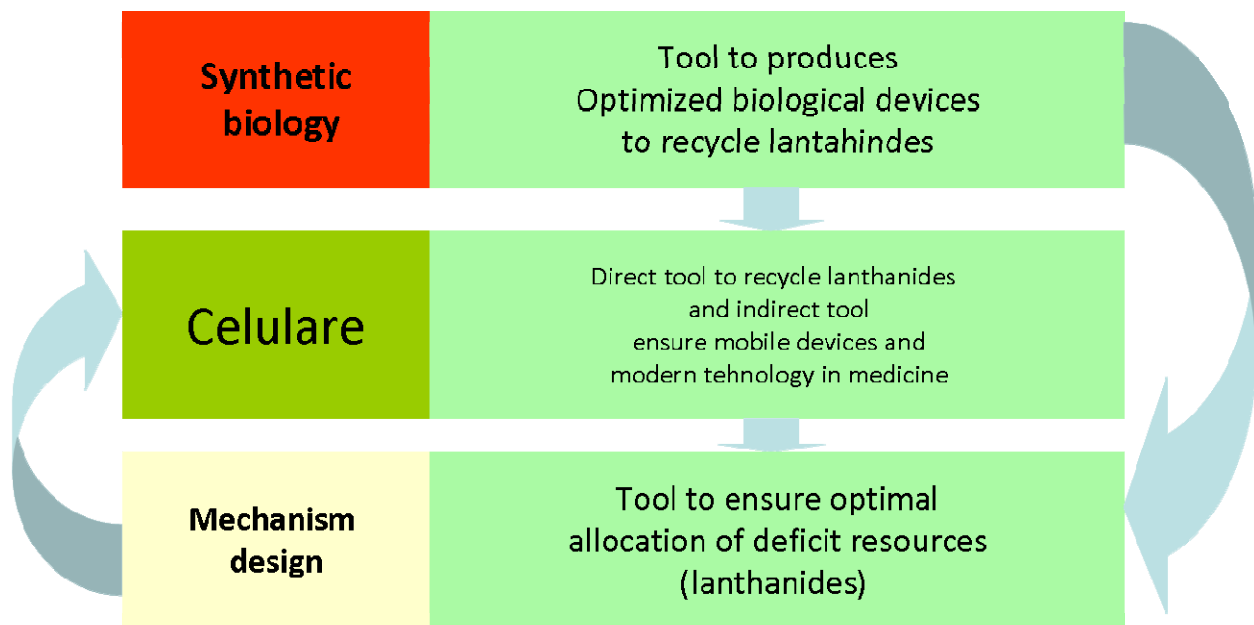
*“The theory of mechanism design can be thought of as an engineering part of economy. Much of theoretical work focus on existing institutions. The theorists want to explain or forecast economic or social outcome that this institution generate. Mechanism design reverse the direction it begins by identifying desired outcomes (goals) and continues with asking if*

*institution can be designed to achieve in order to achieve those goals?” said Erick Maskin (Nobel Prize Winner) [1]*

Mechanism design (reverse game theory) is a field of economy that focus on creating new incentives and rules for economics aimed at realization of utilitarian social goals rather than personal pursuits. Hence, it may transform healthcare allowing to better design markets as well as redesign of institution itself, which ensures more efficient way of allocation of deficit resources. Mechanism design theory focuses on analyzing the way in which institutions efficiently allocate public goods and services. It optimizes systems by reducing selfish behavior of some individuals. Since we aim for efficient allocation of the resource, mechanism design seems to be a good support for rational decision making in incomplete information state. It may identify efficient trading mechanisms, regulation schemes and voting procedures on healthcare market.

## **Celulare: transforming healthcare for optimal allocation of deficit resources**

We recognized both biological and mobile devices as tools to providing advanced technology to healthcare in a cost-reduced manner. As ‘Celulare’ is focused on lanthanides bioremediation, we want to propose strategy to optimal allocation of these elements and other deficit resources on healthcare market. ‘Celulare’ could be treated as an example how to implement a comprehensive strategy to achieve these goals by means of synthetic biology, medical technology and mechanism design tools merged together (Figure 2). Later, this strategy would be applied by hospitals via Lanthan Recycling System.



**Figure 2. Celulare: transforming healthcare for optimal allocation of deficit resources**

### *Lanthan Recycling System for Hospitals*

The very idea of Lanthan Recycling System for hospital derives from the fact that lanthanides are nowadays deficit resources with broad application including medical industry (Figure 4). 'Celulare' has been aimed at design a bacterial system capable of detecting and binding lanthanides in order to extract these ions from electrowaste, thereby recycling these valuable metals more effectively. In other words, the long term goal was to introduce an eco-friendly retrieval technology for metal extraction. Then we envisaged that our system can be applied also in healthcare, since it extensively use lanthanides in technologically advances devices and therapies.

## **Future Lanthan Hospital - implementation strategy through 'Celulare'**

As it was mentioned before, on the basis of Lanthan recycling system we created model of Future Lanthan Hospital - healthcare institution fully supplied with modern technologies based on rare-earth metals (lasers, surgical robots, MRI, etc.) as well as with mobile and telemedicine technologies (Figure 3. A). Furthermore, we tried to define specific target groups of interests for this model. As much as we are concerned, those groups are wards and healthcare centers workers, which require lanthanide-based technologies (Figure 3.B). Thus, they could benefit mostly from practical implementations of our recycling system.

### **Specific target group 1 : oncology professionals**

#### **Modern oncology center - transforming oncology with Celulare**

MRi and Molecular Imaging including molecular MRI (advanced visualization in oncology)

Surgery Robots and Medical Lasers (surgical oncology)

Novel therapies in oncolgy (photodynamic therapy)

Telemedicine, Smartphones and tablets for medical doctors (large amount of data - genetic disease and long-term systemic treatment)

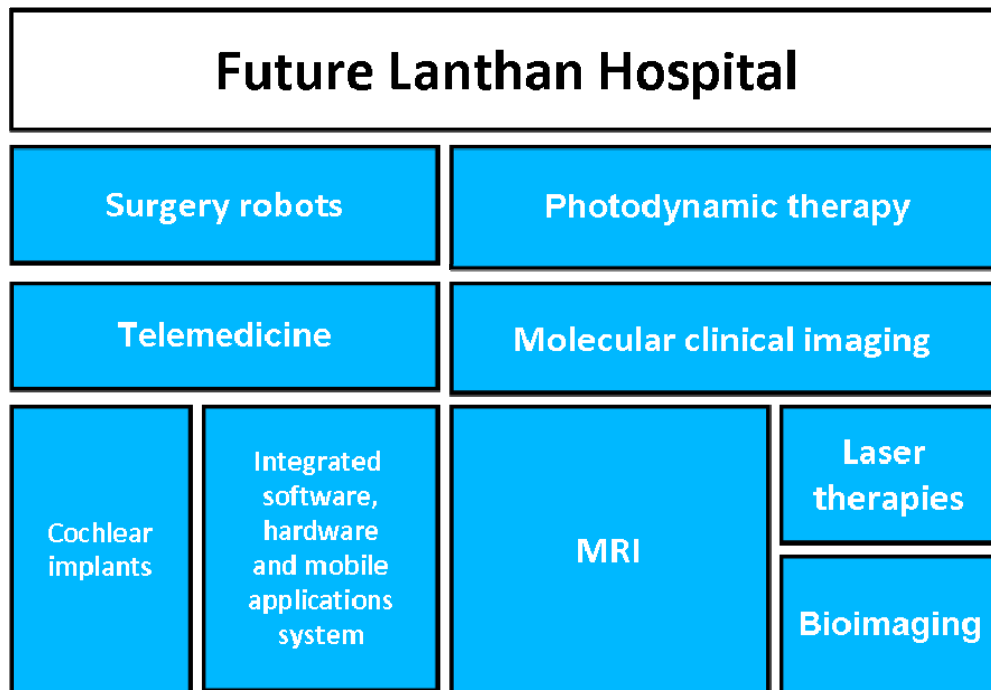
### **Specific target gropup 2 : Audiophonology professionals**

#### **Modern hearing center - transforming audiophonology with Celulare**

cochlear implants, MRI, bioimaging, teleaudiology

A.

## Biomedicine and bioengineering in patient service



B.

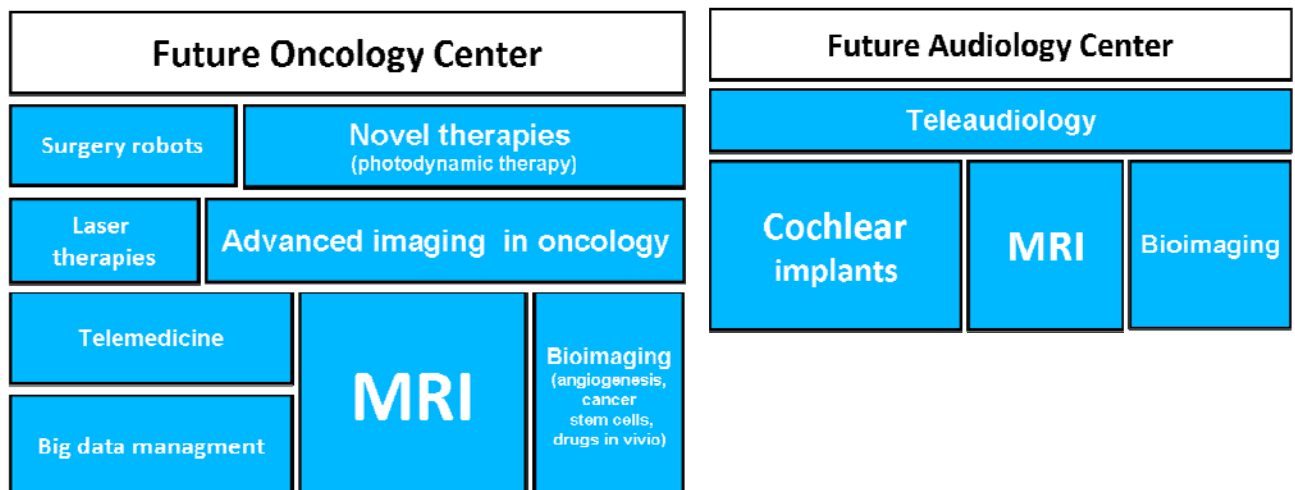


Figure 3. Future Lanthan Hospital – idea of lanthan- based technology which pieces can be perceived as Lanthanbrick for Lanthan hospital. A. “Building” future hospital with modern biomedical technology and IT solutions from “LanthanBricks”. B. “Building” future wards and future medical centers on the basis of Lanthan- based technology



## **Celulare Recommendations:**

**Firstly, we recommend to use interdisciplinary tools designed using biological, medical and economical principles in integrated, complex manner.**

**Specific Celulare Concept:** If we intended to supply a hospital with medical devices and our funds are limited, we should forecast what hospital could possibly exchange with medical companies to get their products. Such idea may be consider as a kind of barter trade. As most of our desired products contain lanthanides (which are deficit resources on global market), becoming a provider of lanthanides appears to be an excellent solution for hospitals. However, currently available extraction methods are rather cumbersome and expensive, thus a cooperation with synthetic biology lab could ensure cheaper method of their recycling from electrowaste. If new industrial methods are developed (with hospital support), such strategy could benefit in financial gains and access to modern technologies. Nevertheless, it requires development of a proper business model. We suggest that hospital should introduce appropriate law regulation based on mechanism design theory not only to prevent selfish behavior in the decision making process, but also to achieve optimal allocation of following resources: funds, recycled lanthanides and gained medical equipment.

**Secondly, we would like to propose a strategy allowing the healthcare industry and helth-tech startups to work together.**

**Specific Celulare Concept:** We believe that there is one lacking element crucial for cooperation between technological companies and hospitals with integrated synthetic biology lab. Namely, a presence of startup companies allowing to a barter exchange process of lanthanides and medical devices. Such a hypothetical company should also insist on collaboration with industry to initiate lanthanide recycling on the large scale. This allow to exchange recovered lanthanides with tech-oriented companies. Afterwards, these companies should equip the hospital with modern technologies based on lanthanides.

**Third, we would like to propose transfer of modern economic concepts to healthcare market promoting startups focused on resolving optimal allocation problem.**

**Specific Celulare Concept:** As lanthanides are deficit resources, they required proper allocation on healthcare market and, by similarity, lanthanide-based technologies needs proper allocation inside hospital. Lanthanides have broad application in many medical devices and technologies, which are provided by different companies. Therefore an efficient kind of auction should be designed in order to exchange lanthanides. According to previous paragraphs, we recommend implementation of mechanism design theory in negotiations between companies to ensure the most efficient way of bargaining and achieving more social-oriented goals - making technologies more accessible for patients. In next stage it is necessary to think about optimal allocation of medical devices in the hospital - preferences of different wards must be taken into consideration. In this case stable matching algorithm should be applied. Suggested method is expected to provide much people with resources they really need. Thus, in case of implementation of Future Lanthan Hospital model, we propose a solution inspired by the Nobel Prize in Economy, which we termed "Nobel Lanthan Economy".

## **Nobel Lanthan Economics with Nobel Human Practice**

### **→ Eric Maskin (Nobel Prize in Economics 2007): mechanism design**

Maskin is a Nobel Prize winner, who has contributed to foundation of mechanism design theory. What is more, together with James Bessen [2], he argued 'innovation is "sequential" (so that each successive invention is built on the success of its predecessors) and "complementary" (so that each potential innovator takes a complementary research strategy)'. Their sequential model of innovation is supported by evidence from a software industry, in which imitators can provide benefit to both the original inventor and the whole society.

### **New Application: mechanism design through iGEM for healthcare market**

iGEM philosophy bears a resemblance to Maskin's view on achieving social goals, and it is based on competition-driven strategy leading to better results. In the first step of Future Lanthan Hospital Model we would like to develop IEDMs to change the attitude of medical communities to open source philosophy. It is beneficial to use Maskin's theory to accomplish some social goals, such as developing an iGEM Human Practise for hospital.

### **Celulare Application: providing a proper solutions and law regulations in negotiations between healthcare startup and giant tech companies**

We aim to develop a startup-like model of healthcare institution which additionally has a system impact on the industry. As we mentioned before, the mechanism theory should reduce selfish behavior of both parties involved in business negotiation. According to works of Brahm and Mittis [3], a proper use of mechanism design principles is able to impose honest bargaining. The following excerpt from their seminal paper [3] shows the basic idea:

*"A classic challenge in contract and property law is unstructured negotiation between two parties with asymmetric information (i.e. each party has different private information) under bilateral monopoly (each party must negotiate with other to try to reach an agreement), which often leads to prohibitively high transaction costs, and if the parties fail to agree, social costs as well. In this situations law should incorporate principles of mechanism design, a methodology which employs structured procedures to give the parties incentives to reach agreement. In terms of contract theory, mechanisms constitutes algorithmic altering rules that reduce, if not eliminate, inefficient transactions." [Law and mechanism design: procedures to induce honest bargaining ]*

The enormous challenge and long term goal for the Future Lanthan Hospital Model is to provide a valuable contribution in the introduction of law regulation based on mechanism design.

## → Alvin Roth (Nobel Prize 2012 in Economics): stable matching algorithm for healthcare - mechanism design without money

Alvin Roth demonstrated that stability is the key to understanding the success of particular markets, including healthcare market. He has adjusted stable matching algorithm to real practical problems. In this context, stable matching refers to finding an optimal superposition of two sets of elements, given a set of preferences for each element. Stable match in which there is no incentives to “change” any matching, is to achieve by usage of top trading cycles algorithm. It’s principle is very simply and is based on an initial allocation of objects and subsequent swapping [4]. Roth adapted that theory to real problems in healthcare. His examples include the assignment of new doctors to hospitals and human organs for transplantation. The last one is called Kidney Paired Donation (KPD) [4]. So in fact, Roth received Nobel Prize for showing the best way to match people with what they really need. As his contribution refers to kidney transplantation, he is perceived as an economist whose work actually saves people lives. Even Roth said *“Well, you know, market design is a helping profession, we help our surgical colleagues to save some people’s lives.”*. We are aimed at using his theory in business model for startup company, but in first stage of transformation we are about to test it in Human Practice for Future Lanthan Hospital. To conclude, our dream is to match patients with things they really need.

### **New application: developing business model for startup company which exchange goods or conduct auctions**

Roth findings provided ground for further analytical developments as well as practical design of institutions. One of the main feature of these improvements refers to situation when prices are not a part of matching process. From the ethical point of view, prices itself should not be used to allocate deficit resources. However, algorithms which include prices work in similar manner and they may produce stable matches. In fact, price matching is closely related to auctions,

where objects are matched with buyers, hence prices are decisive [4]. Researchers who relate matching algorithms to auction, recently published interesting theoretical results, which appear to be applicable in practice [4]. Interestingly, some companies have already gained some profits from application of aforementioned algorithms in practice [4]. As Makin's mechanism design is directly connected with the auction problem, we would like to point out some connections between this two theories. According to our believe it is beneficial to integrate these theories in business development for startup companies which exchange goods or conduct auctions.

### **Celulare application: ensuring proper wards and centers in healthcare institutions with what patients really need**

We would like to propose to use Roth's findings in developing our Future Lanthan Hospital model. It can be noticed that exchanging lanthanides for medical devices is similar to barter trade in kidney paired donation problem or during some auctions (depending whether chosen business models presumes using prize), so adaptable matching algorithm could be useful. What is more, when medical devices are gained for hospital, we will want to allocate them in possibly optimal way (including preferences of particular wards, centers and MDs determined by the patients needs).

### **Stable matching and mechanism design through Celulare to Polish healthcare market**

Since we are focused on our long term goals - implementation of Future Lanthan Hospital Model, we would like to promote transfer of mentioned economic concepts to Polish healthcare market, by connecting our project 'Celulare' with promotion of beneficial economic concepts in Poland. We would like to promote mechanism design via 'anti selfie mechanism design for smartphone MDs by 'Celulare' action connected with Future Lanthan Hospital Model (see annex 1). It will allow us to promote a notion of combining modern technology with rational and eco-friendly profile of institution as well as rational allocation of resources. The second economic conception - stable matching algorithm, will be supported and promoted by

project on implementation of KPD in Poland (see annex 2). That actions should help with changing the attitude of society, especially medical community's to the idea of sharing and openness. By KPD project, we want to emphasize direct economical gains from changing the attitude. Simultaneously, we would like to point out that optimal allocation of resources needs more open access to data. During development of KPD project, we fully realized problems concerning data structure and limited access to them as well as openness of medical professionals.

### **Closing remarks**

To sum up we would like to encourage to seek new possibilities of collaboration of the interdisciplinary projects through new ways of communication in science. First we are going to improve our project to make it suitable for further collaboration. This is to achieve by support of Scientia Crastina (latin for 'The Science of Tomorrow') which is a networking platform for the discussion of scientific communication and science communication. This way we can make our ideas clear for people of different background (economics, law). We have started so far collaboration with members of Collegium Invisibile and the program 'Leaders of healthcare market' supported by Foundation 2065 im. Leśław A. Pagi (see annex 3) so we need to prepare our language in the way facilitating further actions and performing some analysis to develop business model for Lanthan Hospital. That is why we have proposed a solution to facilitate the data acquisition, simultaneously changing the social attitude towards transformation of the healthcare. We would like to use that data to perform several analysis connected to Future Lanthan Hospital.

Finally we would like to put emphasis on creative medical education with interdisciplinary approach to find future MDs on the border of sciences iGEM Team members have prepared workshops for highly gifted students interested in biology and medicine (see annex 4) We wanted to spread the idea of Future Lanthan Hospital and potential applications of lantahnides in medicine, as we thinking of our long term goals from the beginning - we want our project Celulare to have real application and meet people needs and contribute to transforming

healthcare through synthetic biology approach. We need to address future leaders and prepare them for collaboration in interdisciplinary projects on the boundaries of science, business and technology. We need new way of communication in science to make big dreams real.

### **Acknowledgments**

We would like to thank Piotr Dworczak for inspiration of mechanism design theory and crucial contribution to project on estimation of potential gains from implementation of KPD pilot program in Poland. What is more, we would like to acknowledge Piotr Byrski for cooperation in workshops on Future Hospital and Piotr Migdał for providing us with the cover photo.

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## **Annex1.**

### **Anti selfie mechanism design for smartphone MDs through Cellulare**

We strive to launch the action we called "anti selfie mechanism design for smartphone MDs". The idea behind the action is to combine modern technology and pro-ecological design, in order to improve the work of healthcare.

#### **Specific Cellulare Motivation**

It is obliged to perform some analysis on rational decision making before starting the business model for Future Lanthan Hospital. As we are dedicated to implement this model in Poland at first, we need to have broad access to medical data, which will allow us to make first estimation of the costs. Another step will be providing more detailed law and environmental analyses. Therefore, we would like to encourage individual MDs, healthcare institutions and high-tech companies to reveal some data and to cooperate in our action 'Anti selfie mechanism design for smartphone MDs through Cellulare'.

According to what was presented in previous paragraph, we intend to educate medical community (and also the whole society) on synthetic biology, open source science, data structuration and optimal allocation of resources by mechanism design. We also aim at changing the mental attitude to data analysis and show some benefits of open access to information. We intend our action to be supported by healthcare tech companies. Thanks to this we hope to gain some valuable data and contribute to better understanding of economical, legal and social context of transition to more open society. That knowledge would be useful in



implementation of our project, especially by cooperation with members and Alumni of the program 'Leaders of healthcare market', supported by Lesław Paga Fundation 2065.

### **The plan for the action:**

#### **First Stage: targeting society - to match patients with their real needs**

We would like to show beneficial changes for society, resulted from implementation of modern technologies in medicine, by educating people about applications, safety and some security problems related to cutting-edge technologies.

We need to find answers for following questions:

- what is the attitude of the society to smartphone based diagnostics?
- what is the attitude of the society to other lanthanide-based technology?

Surveys are to be performed before and after our educational action.

#### **Second Stage: targeting medical community to match MDs with their real needs**

We would like to educate MDs about modern technologies in medicine to show the potential of synthetic biology and modern economic concepts, which should facilitate cooperation of medical community with both science and business.

By educational action for medical professionals we hope to estimate:

- How many MDs are using smartphones and tablets for professional purposes?
- How many MDs would like to use smartphones and tablets in hospital for professional purposes?

- Which lanthanide-based technologies they would like to use?
- What is MDs attitude to synthetic biology and modern economic concepts?

Surveys are to be performed before and after our educational action.

### **Third Stage: Targeting medical companies with their needs**

We would like to cooperate with the companies to increase the range of their recipients and to extend the market for them by taking into account the real needs of patients and MDs.

We would like to obtain following data from tech companies:

- Which lanthanides and their alloys are used in medical devices?
- What are the production and exploitation costs of some lanthanide-based devices (and the usage of therapies requiring lanthanides)?
- What is the source of lanthanides?
- What is the demand of health tech companies for rare earth elements?
- How the demand is going to change in the future?

### **Our goal and desired effect:**

We would like to find the answer to the questions concerning the role of lanthanides in development and implementation of mobile technologies in medicine. This knowledge would contribute to broader analysis of the usage of mobile solutions by healthcare market in Poland.

We aim to estimate what is the potential cost of equipping Polish MDs with smartphones and tablets with integrated diagnostic software. Moreover, it might be interesting to know if that solution is cost-effective or not. Similar estimations could be done for lanthanide-based technologies. However, the major challenge would be to estimate both current and future demand for such technologies.

## **Anex 2. KPD - optimal allocation of deficit resources need access to databases**

Idea of the project 'estimation of potential gains from Kidney Paired Donation and comparative analysis of national and worldwide transplant law to facilitate implementation of a pilot KPD program in Poland [1]' reused and show from novel perspective by iGEM Team Warsaw with permission of authors

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Kidney paired donation (KPD) has emerged as an innovative option for recipient and their incompatible donor to be paired with another donor and recipient. Usually exchange involves two pairs; however longer cycles are also possible. The algorithms to optimize the use of live donor organs (see Figure 2) has revolutionized the way kidney transplants are performed in the USA. Modified top-trading-cycles algorithm has been used for solving optimal allocation problem for kidney exchange in longer cycles. This was to ensure the maximal number of transplant taking into account the compatibility between donors and recipients. If we want to optimize matching to ensure the highest number of conducted transplants it can't be achieved in random way – as each match do means – algorithms support the process and ensure optimal choice. The growing source of transplantable kidneys is achieved by construction a national KPD system operated by the Organ Procurement and Transplantation Network, administered by United Network for Organ Sharing. Several other countries has been attempting to implement KPD, however exchange does not take place on a large scale. The negligence is attributed to the strictness of law and the absence of economic analysis of the situation. So far no such program has been launched in Poland.

**Keywords:** kidney paired donation, transplantation law, matching theory

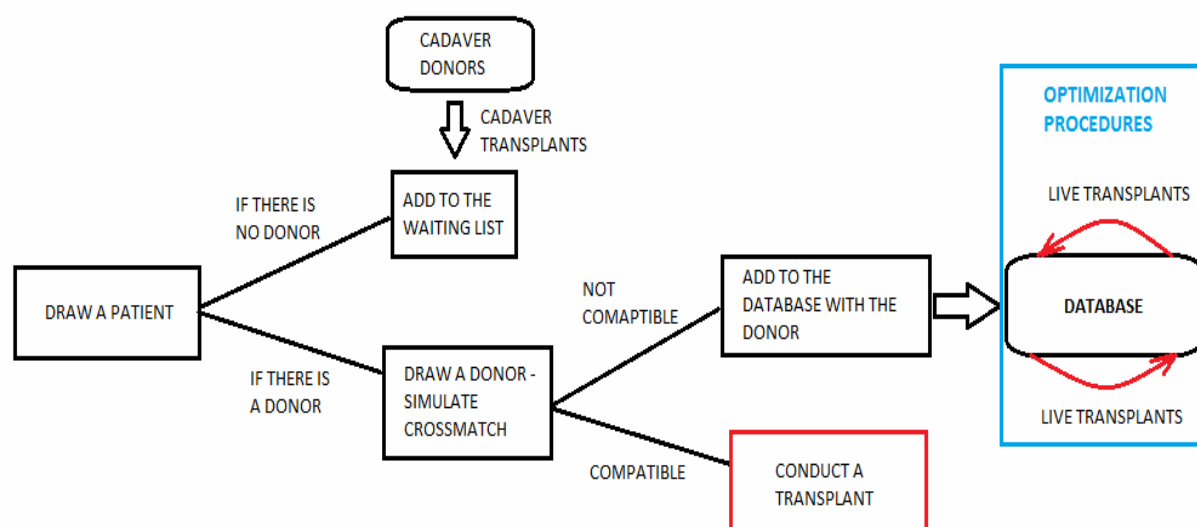
**Aim of the study:** The main aim of the study was to estimate potential gains from introducing KPD, point out legal barriers and propose changes in transplant law to pave the way for constriction of KPD program in Poland.

**Material and methods:** The study consists of two parts: model developed on the basis of medical data and a comparison of Polish transplant acts with global regulations. In the first part we run a simulation (figure 1) in which we draw a sample of patients and donors (along with their relevant characteristics) using available data, including Poltransplant data, to calibrate the parameters of the distributions (tabela 1).

**Figure 1. The model of the Kidney paired donation simulation**

STEP 1: Estimate/calibrate the distributions of patients' and donors' characteristics using existing data

STEP 2. Generate (drawing from the estimated distributions) a database of patients and donors



STEP 3. Compute the number of transplants conducted in different systems

STEP 4. Repeat step 2) and 3) N times (where N is large)

Compute the average number of transplants in every system

To reflect recipient-donor compatibility we use PRA (percent reactive antibody) parameter. Then for a given database of patients and donors we check how many transplants would be conducted under different regimes (cycles of 2, long cycles, stable matching and benchmark). As the baseline regime we use the system that is currently being used in Poland. We test several different systems that allow for indirect kidney exchange using algorithms from matching theory (economics).

**Table 1. Simulation with medical data, including Poltransplant reports.**

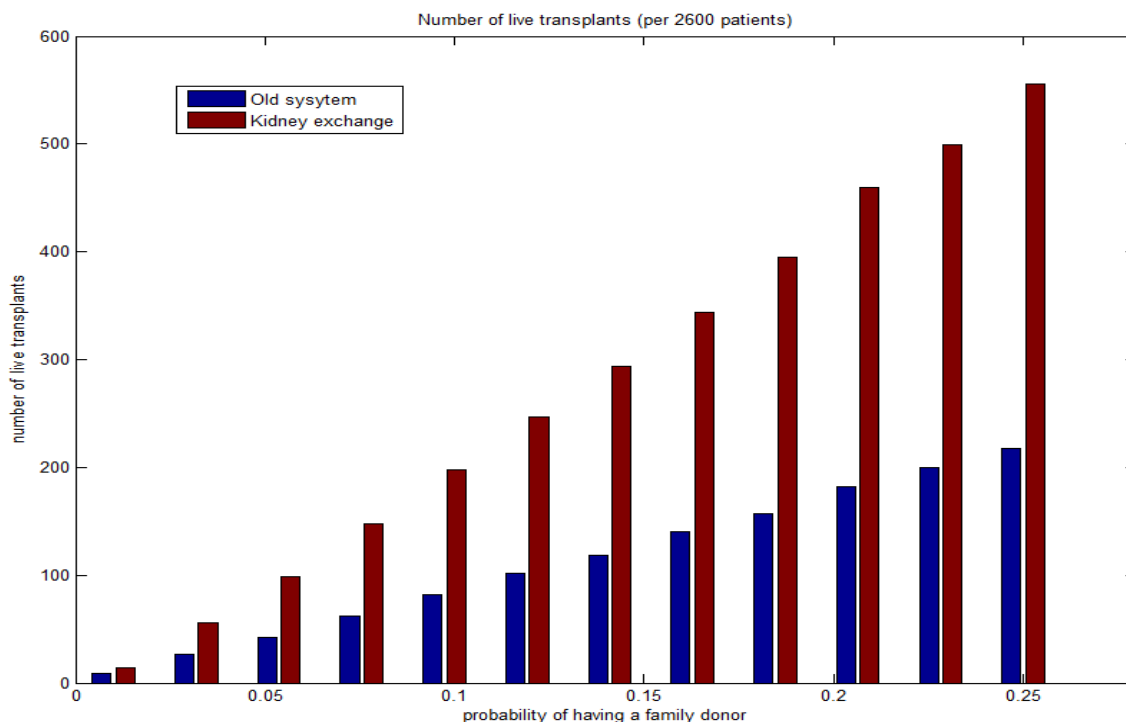
Name of variable	Estimation methodology	Results
Age	Method of moments (assuming lognormal distribution)	Lognormal with $\mu=3.8$ and $\sigma=0.32$
PRA	Simulation to match moments (assuming the distribution is a mixture of uniform distributions)	Uniform on $[0, 0.5]$ with prob. <b>0.94</b> Uniform on $[0.5, 0.8]$ with prob. <b>0.04</b> Uniform on $[0.8, 1]$ with prob. <b>0.02</b>
Blood Type	Directly from data	-
Probability of having a donor	Simulation to match data	<b>Prob. 0.05</b>

**Results:** preliminary results from Monte Carlo simulations indicate that the gains from using pairwise kidney exchange are huge - it can lead to more than doubling of the number of conducted transplants (table 2). Interestingly because of less differences in PRA distribution for Polish population compared to American population which characterize more versatile PRA, gains from cycles of length two may ensure increase in the number of conducted transplants similar to those achieved with stable matching algorithms in longer cycles of transplantations. This is good news as this means that implementation of KPD in Poland could be even more cost effective than in USA as transplants with shorter cycles require less surgery rooms available and less complicated is the system enabling conducting transplants between transplant centers

**Table 2. Potential gains from KPD in Poland assuming different allocation systems.**

Method	Average number of live donor transplants (for a database of 2600 patients)	Average relative gain in live donor transplants
LONG CYCLES	<b>103</b>	<b>2.5</b>
CYCLES OF LENGTH 2	<b>90</b>	<b>2.2</b>
STABLE MATCHING	<b>95</b>	<b>2.3</b>
BENCHMARK	<b>41</b>	-

in different regions of country Also law procedures are easier to introduce. Here we would like to add that adaptation of Charlie W. Norwood Living Organ Donation Act could facilitate launching of KPD program in Poland. In the end, there is one more interesting observation that even if the probability of having a donor increases, number of conducted transplant is going to constitutively increase with KPD (Figure 2). Those encourage to launch such program in Poland to ensure more transplants.



**Figure 2. Effects of increasing the probability of having a donor (for the Stable Matching algorithm).**

**Conclusions:** Our findings from the simulations are valuable for encouraging participation of polish transplant centers in the program. Establishing a national registry for paired exchange would provide more opportunities to save and enhance people's lives. The legal status of kidney exchange in Poland requires additional records prior to the KPD implementation As a conclusion not only lack of economical and law analysis is an obstacle to implement novel healthcare programs in Poland but also lack of medical data structured in a way to facilitate building simulation models. This is way we perceive collaborate with iGEM Warsaw Team as valuable to transform healthcare for data anlysis.

[1] On the basis of abstract from conference materials: "Estimation of potential gains from Kidney Paired Donation and comparative analysis of national and worldwide transplant law to facilitate implementation of a pilot KPD program in Poland" - "Archives of Medical Science" vol. 9, issue 2, 2013 (suppl.1autorzy: Anna Kornakiewicz, Piotr Dworzak) - Termedia Publishing House -04.2013 - ISSN 1734-1922, eISSN 1896-9151.

### **Annex 3 .**

## **Cellulare - future leaders start here**

We hope to improve our model by means of cooperation with members and Alumni of the program 'Leaders of healthcare market' supported by Foundation 2065 im. Lesław A. Pagi and Collegium Invisible members.

Members of the program of 'Leaders of healthcare market' have an exceptional opportunity to attend prestigious internships in best healthcare institutions and companies in Poland. After internship completion, they would share their gained knowledge and experience with iGEM Team Warsaw, helping us to develop Future Lanthan Hospital Model. This is a way to enable people from different backgrounds (law, economy etc.) to contribute to our project.

We are also about to launch a pilot program aimed at cooperation between Collegium Invisible and iGEM Warsaw Team members. Collegium Invisible is an academic society in Poland, which members are outstanding Polish students working with distinguished scholars from various disciplines. The society's supreme idea is to provide a worthy contribution to the welfare and development of Polish science. An example of that attitude is the promotion of sharing knowledge and experience among students. So its idea is very similar to iGEM philosophy; Collegium also aims at offering young scholars the opportunity to participate in academic research projects as well as exclusive individual master-student cooperation through the tutorial system. Our aim is to establish mutual cooperation with the Collegium Invisible by active support of iGEM Team Warsaw projects. The first interdisciplinary project that was launched involved estimation of potential gains from implementation KPD Pilot Program in Poland. Currently, the project is further supported by iGEM Team Warsaw. The second collaborative project was aimed on organization of interdisciplinary workshops on Future Lanthan Hospital for gifted students for Polish Children's Fund. The Polish Children's Fund is an independent, non-governmental organization. One of its major objectives is to help



exceptionally gifted pupils and students in development of their either academic or artistic skills and to adjust the educational system in Poland to accommodate the special needs of the gifted children. Members of both iGEM Warsaw Team and Collegium Invisible wish to contributed to open creative education, hence our long term goal is to build a group of passionate students who will continue spreading our ideas in the future. In these particular cases we feel an obligation to help in STEM education in medicine and to find some future leaders to take care of Lanthan Hospital Model (and iGEM team in general). We also hope to perform several analyses related to our project in cooperation between iGEM team and mentioned organizations.

#### **Area of collaboration:**

We intend to match people with their needs, hoping that this will allow them to fulfill their ambitions and develop their potential. Hence, we do not have any fixed ideas about the nature of our possibilities - we only provide general conception. Some open questions are still left - to be developed, according to the preferences and the original ideas provided by our collaborators themselves.

#### **Cost-effectiveness analysis**

**Problem 1:** When our project 'Cellulare' is fully developed, we also would like to provide cost-effectiveness analysis for synthetic biology lab performing our project. We will provide estimation of the cost of materials and equipment required to finish the project. After the development of the industrial process, a comparison of costs between our methods and existing technologies would be necessary. Support from people having economic background will be appreciated.

Support: by students with economic background.

## Law analysis

**Problem 1:** Important question is how to adjust the regulations necessary to integrate synthetic biology lab with hospital? Is it possible to just establish a synthetic biology lab in the hospital or are there any additional requirements which need to be fulfilled?

**Problem 2:** Do we need a straightforward way to introduce some legal regulation based on mechanism design in order to achieve social goal we mentioned in previous chapters? How to introduce legal regulation enforcing honest bargaining to prevent selfish behavior and ensure optimal allocation of goods?

In both cases, the support from people having an expertise in Polish law would be beneficial.

## Security and Ethics

**Problem 1:** Discussion on ethical issues (including safety) of the synthetic biology methods for medical purposes. DIY (Do it Yourself) versus common medical standards - how to meet the public's expectations about the credibility, reliability and professionalism.

**Problem 2:** Open flow of information versus security of personal data. New concept of medical hacker.

The debate on mentioned problems will be supported by people from humanities (Collegium Invisibile).

## **Environmental analysis - 'ecological hospital, green economy'**

**Problem 1:** It is crucial to estimate the potential threats to the environment caused by electronic waste, especially taking into account the hospital electronics, eg. MRI. We need to discuss the environmental impact of recycling methods provided by our project.

The analysis would be supported by people with engineering and environmental background. Also a person with economical background is needed.

Our Team contribution to analysis is below.

Author: Agnieszka Samsel

### **E-waste, the scale of problem**

Electrical and electronic products have become ubiquitous of today's life. Without them modern life can not be possible in most of the countries. *The StEP* definition of EEE is: „Any household or business item with circuitry or electrical components with power or battery supply” We use EEE (Electrical and Electronic Equipment) in medicine, health, food-supply, communication, security and culture. [1]

Waste of electrical and electronic equipment is considered to be the fastest growing waste stream in EU (3-5% per year). [1]

	Products put on the market	Waste collected from households	Waste collected from other sources	Waste collected	Treated in the Member State	Treated in another Member State of the EU
Large household appliances	105 996	50 410	301	50 711	32 146	17 272
Small household appliances	63 930	11 762	30	11 792	10 456	0
IT and telecommunications equipment	72 666	17 424	1 867	19 290	18 532	385
Consumer equipment	27 799	26 312	10	26 322	25 416	0
Lighting equipment	26 258	1 574	69	1 642	1 642	0
Gas discharge lamps	4 018	1 362	0	1 362	1 362	0
Electrical and electronic tools	14 898	2 572	39	2 611	2 611	0
Toys, leisure and sports equipment	4 781	351	1	351	351	0
Medical devices	3 733	51	288	339	337	0
Monitoring and control instruments	2 761	131	69	200	200	0
Automatic dispensers	2 760	0	1 838	1 838	1 519	0

**Table 1. EEE put on the market, collection and treatment of WEE, 2012, European Union [tones] [3]**

In 2012, in EU, 329 600 tons of EEE were put on the market, but only 116 458 tons of them were collected. Households are the main producers of WEEE. Most of the garbage are large and small household applicants (44+ millions put on the market), IT and telecommunication equipment. Standard time of exploiting EEE is 3-5 years. [1]

In 2009 each U.S. house has at least four small ( $\leq 4.5$  kg) and between two or three big ( $>4.5$  kg) e-waste items in storage. That gives 747 million e-waste items, weighing over 1.36 metric tons. [2]

WEE which are not recycled drift to landfills, but not all stay in Europe or USA. Many of e-waste is transported to China, Ghana, Pakistan or Nigeria where fly dumping is cheaper and law is not as strict as European or American one. [3]

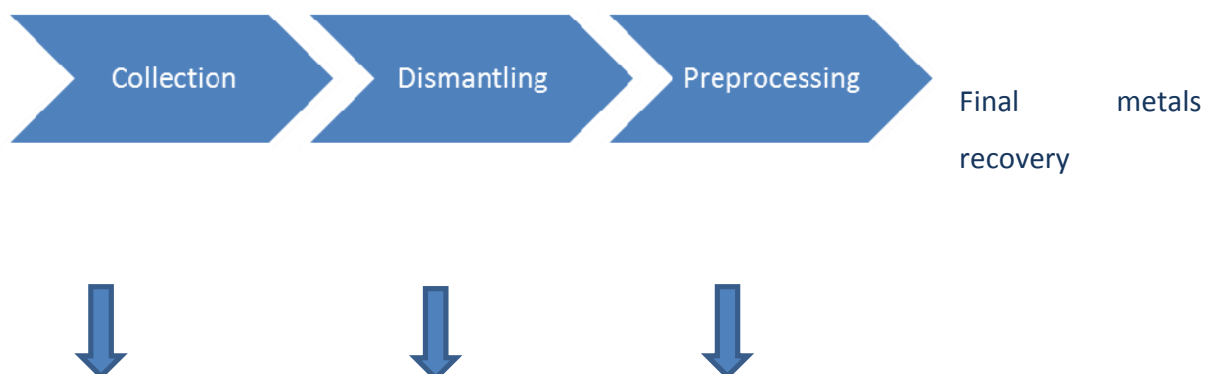
## E-waste, problem of the whole world

Not only EU and United States have a problem with WEE. Nowadays we have to face with e-waste in developing countries. Developed countries, especially in EU, have very strict legislation with recycling WEE. Manufacturers take back items collected by retailers or local government to safe destruction or recovery of materials. Things which are prohibited in EU, are easy to do in developing countries such as India or countries of West Africa. [4]

The developing countries become a toxic yard for dumping e-waste. Lower environmental and labor standards and relatively high value of recovered metals transfer to making developing countries more attractive to recover some kind of metals. Shipment is often through middle man, under tariff classifications that make quantities difficult to access. Despite the interest of national regulations and waste laws, most of e-waste is treated as general refuse, by burning or acid baths, with recovery of only few meals (lanthanides are rarely recover from e-waste). Heavy metals, toxins and chemicals leak trough landfills into surrounding waterways, poisoning local people. [5]

## What we want to do?

Our process does not need many workers to support. It is also environment friendly and we recover rare metals without using acid or high temperature.



**Collection** of e-waste is crucial and determinates the amount of material which will be recycled. It depends more on the social factors than on collection methods.

In **dismantling** and **preprocessing** we want to liberate e-waste and direct them to adequate treatment process.

**Final metals recovery** is a process where we use our lanthanides binding bacteria.

The efficiency of the entire recycling chain depends on the efficiency of each step and on how well the interfaces between these steps are managed. Efficiency of each step mostly depends on the WEE witch we want to recycled. [1]

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2. Ogunseitan Oladele A. et al., *The Electronics Revolution:From E-Wonderland to E-Wasteland*, Science(2009), 326, 670-671,
3. Schluep Mathias et al., *Recycling from e-waste to resources* , StEP, 2009
4. Suthipong Sthiannopkao et al. , *Handling e-waste in developed and developing countries: Initiatives,practices, and consequences*, Science of the Total Environment 463–464 (2013) 1147–1153
5. Wong, M.h. et al., *Export of Toxic Chemicals – A Review of the Case of Uncontrolled Electronic-Waste Recycling*, Environmental Pollution 149.2 (2007): 131-40

## Annex 4.

### Creative education - workshops

Workshops for students from “Highly gifted” program of Polish Children Fund prepared by members of Collegium Invisibile and iGEM Warsaw Team 2014 with a view to introduce idea Future Lanthan and simultaneously fascinate young people with synthetic biology and show idea of startups. Hospital workers show advanced lanthanides based techniques of visualization in oncology. We also prepared workshops on advanced visualization in oncology (molecular imaging, MRI) to show applications on lanthanides in medicine and collaboration on the boundaries of science.

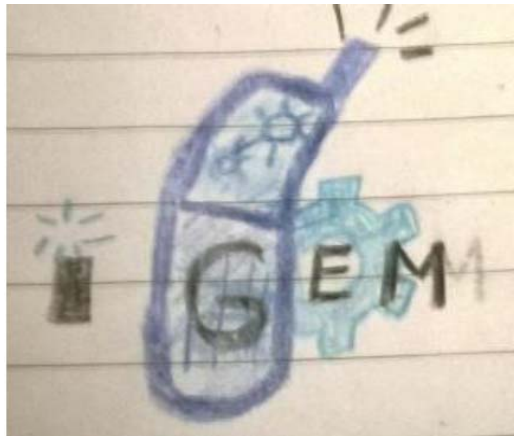
**Field:** Medicine, Synthetic biology, Entrepreneurship

1. The Future Hospital – new technology and visionary ideas serving public health
2. ‘Visual Oncology’ – can you imagine cancer?



Photo:Piotr Migdał, used with permission

## The Future Hospital – new technology and visionary ideas serving public health



All-development workshops, 27-28 April  
17:00 -18:30

Anna Kornakiewicz<sup>1,2,3</sup> Piotr Byrski<sup>1,3,4</sup>

*Life bits!*

*To ensure best healthcare possible, the doctors need the best technology available. Mobile medical devices, applications, software and hardware revolutionize the view of a hospital. These days, with the aid of IT you can evaluate the heart function and image lungs as swift as you check your email!*

**Day 1. What is this “Future Hospital”?** –discussion about existing solutions. We will talk about some of the already active medical start-ups. (**Quantitative Healthcare**: medical devices like stethoscope, ultrasonograph—all smartphone-synchronizable, **Biomeme**: smartphone medical laboratory, **Nanthealth**: a clinical system based on cloud computing etc.) We’ll end the day with a short introduction to our plan for Day 2.

**Day2. Harder, better, faster, stronger.** We are already excited for **your visionary ideas!** We will discuss them together. We will also describe two of our start-up ideas, one of which is the **Future Lanthan Hospital**—a hospital modernized by technology based on lanthanides, which is a start-up project of the iGEM\* Team Warsaw2014. That means: how to get raw materials to assemble smartphones and medical devices and how to make them further and more usable for doctors and patients.



## For whom?

For people wishing to get their ideas implemented quickly! For those into healthcare issues, new technologies, smartphone and tablet users. For all of you –to discuss and create ideas, we are going to need people with different backgrounds that like critical thinking and rapid prototyping!

.....  
*\*iGEM-International Genetically Engineered Machine –is a synthetic biology competition taking place at theMIT (Massachusetts Institute of Technology). The main idea is to design“living machines”(Biobrick), using geneticengineering.It is addressed to young scientists(high school/university students), who want to enter the rapidly developing world of synthetic biologyand contribute to its development suggesting new solutionsto make people’s lives better with programmed biological machines.*

1. Collegium Invisibile 2. iGEM Team Warsaw2014 3. Medical University of Warsaw4. The College of Inter-Faculty Individual Studies in Mathematics and Natural Sciences, University of Warsaw

# **‘Visual Oncology’ – can you imagine cancer?**

Anna Kornakiewicz\*

Interdisciplinary workshop, 12 am-1.30 pm, April 25-27<sup>th</sup>

## **Medicine is an information science and art of healing**

*There are many techniques of biomedical imagining used at every stage of diagnostics and treatment of tumours, but also during developing new treatments. Bioimaging is a key part of clinical protocols in oncology, providing structural, metabolic and functional information. Integration of imagining and other types of data helps in taking clinical decisions, but also requires cooperation between doctor, biologist and IT specialist, even visualization specialist and data analyst.*

## **To see and understand**

We will use visual data in order to understand what a cancer is and what a cancer specialist (oncologist) does. We will also try to answer a question why medicine is both information science and art of healing.

The goal of the workshop is learning how to analyze visual data and understanding the role of information in medicine, how to think of medical data and how to use them in treatment, research and science.

### **1<sup>st</sup> clinical day: clinical mems**

Workshop of interpretation of RTG, USG, CT, MRI etc. (hopefully afterwards everyone will be able to show off in front of their grandparents ☺). There will also be an interesting clinical puzzle about use of visual data on every stage of detection and treatment of cancer.

### **2<sup>nd</sup> molecular day: next dimension of cancer**

(more advanced bioimaging techniques in oncology – molecular biology’s and medical data integration workshop)

Tasks showing:

- How and why to create spatial body map?
- How to see cancer stem cells, development of blood vessels and gaining drug resistance on bioimaging photographs?

**3<sup>rd</sup> interdisciplinary day: metavisualisation – how to see and understand the beauty of medicine?**

(about the first audiovisual system to teach medicine)

- Playing with the application,
- Talk about visualization of data in oncology,
- Creating a project of visualization for interactive system, using knowledge from previous workshops.

**For who?**

For everyone interested in medicine and molecular biology, who would like to get a glimpse of cancer in different dimension, but also for people from exact sciences, who are interested in the use of data and for artists, humanists and anyone looking for inspiration!

**Useful knowledge:** seeing, understanding, a little imagination and a lot of enthusiasm!

\*Warsaw University of Medicine, Collegium Invisible, member of iGEM Team Warsaw